DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 10/09/2007. Claim(s) 1, 8-22 and 29-32 are pending. Claim(s) 1has been amended. Claim(s) 29-32 have been added. Claim(s) 1, 8-22 and 29-32 are examined herein.

Response to Arguments

Applicants arguments against the ODP rejection over Application 10/105,826 is not persuasive because Applicant is now arguing based on amended claims, but in view of Applicant's amendments to the claims a modified ODP rejection is now made.

Applicant's arguments with respect to the 102(b) rejection of claims 1-5, 8-11, 20, 22, 23, and 25 as being unpatentable over DeLuca WO 98/41501; claims 1-5, 8, 9 and 21 as being unpatentable over DeLuca 5,945,410; and claims 1-5, 8, 9, 20, and 22-25 as being unpatentable over DeLuca WO 02/05823 have been fully considered but found not persuasive as Applicant is now arguing based on amended claims. Since Applicant has amended the claims, said rejection is hereby withdrawn.

Applicant's arguments with respect to the 103(a) obviousness rejection of claims 1, 6, 7, 11, and 12-19 as being unpatentable over DeLuca (U.S. Patent No. 5,843,928) in view of DeLuca (WO 97/11053) have been fully considered but found not persuasive

as Applicant is now arguing based on amended claims. Since Applicant has amended the claims, said rejection is hereby modified.

Applicants argue that there is not a teaching, suggestion, or motivation in the cited references to administer the 2-carbon-modified vitamin D compounds in the recited form (i. e., immobilized and/or slow release form), at the recited site (i.e., at the site of bone transplant or implant), for the recited purpose (i. e., in order to increase the rate of skeletal repair in a subject having a bone transplant or implant).

This is not found persuasive because Deluca et al. (US) teach that the compound, 2MD is useful for the treatment of disease in human where bone formation is desired. Therefore, this teaching would immediate prompt one of ordinary skill in the art to employ 2MD for the treatment of bone fracture where the improvement of bone fracture healing is truly necessary in order to heal bone fracture. There is a reasonable expectation of successfully treating bone fracture with 2MD, well taught by Deluca et al. that 2MD is useful in a disease where bone formation is desired and improvement of bone fracture healing is needed. The limitation of skeletal repair encompasses bone fractures.

Applicants argue that the administering a compound "for the treatment of disease wherein bone formation is desired" is not the same as administering the compound to increase the rate of repair for a bone fracture by stimulating osteoblast-mediated formation of new bone at the site of the fracture. This is not found persuasive because the mechanism by which the active ingredient gives the pharmacological effect (stimulating osteoblast) does not alter the fact that the compound has been previously

used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same. An explanation of why that effect occurs does not make novel or even unobvious the treatment of the conditions encompassed by the claims.

Applicants argue that the present inventors are the first to show that compound 2MD can be used to stimulate osteoblast to form new bone and until the present inventors demonstrated that 2MD could be used to grow new bone (i.e. that 2MD was an anabolic bone agent), there was no reasonable expectation of success that 2MD could be used to increase the rate of repair for a bone fracture. This is not found persuasive because the effectiveness of 2MD for the treatment of disease in human where bone formation is desired as well as improvement in healing of bone fracture is well known by Deluca et al (US). Applicants' stated mechanism of action of stimulating osteoblast to form a new bone does not change the fact that the administration of the same compound previously used to obtain the same pharmacological effects which would result from the claimed method. The patient, condition to be treated and the effect are the same.

In view of Applicant's amendments, the 103(a) obviousness rejection of claims 1 and 26-28 as being unpatentable over DeLuca WO 98/41501 as applied to claims 1-5 and 8-11 further in view of Chin (U.S. Patent No. 5,976,142) is hereby withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 8-10, 20 and 29-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 8-10, 20, and 29-38 of copending Application No. 10/105826 in view of Bockman et al. (U.S. Patent No. 5,556,645).

The instant claims are directed to a method of increasing the rate of skeletal repair in a mammal having a bone implant or bone transplant by stimulating osteoblastic-mediated growth of new bone at the site of the transplant or implant comprising administering to the mammal a therapeutically effective amount of the same compound formula I in an immobilized, slow release form at the site of the implant or

transplant.

Claims of copending application are directed to a method of increasing the rate of repair for a bone fracture by stimulating osteoblast cells to form new bone comprising administering to a subject in need thereof an effective amount of a compound in an immobilized, slow release form at the bone fracture, said compound having the formula I.

The difference between the instant claims and the claims of the copending application is increasing the rate of repair for a bone fracture. However, Bockman et al. (U.S. Patent No. 5,556,645, column 3, lines 45-57) teach that osteoblast is responsible for regulating the rate of bone formation. As such, the claims of the instant Application and the patented claims would have been obvious variations of the other to one of ordinary skill in the art because both set of claims are directed to stimulation of osteoblast which regulate the rate of bone formation.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 8-22 and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeLuca et al. (U.S.Patent No. 5,843,928(US)) of record in view of Deluca et al. (WO 02/05823A2 (WO)) of record and Bockman et al. (U.S.Patent No. 5,556,645) of record.

Deluca et al. (US) teach the compound, 2-carbon-modified vitamin D (2MD) is useful for the treatment of diseases in human where bone formation is desired and the compound is also suited for treatment and prophylaxis of human disorders such as host versus graft reaction, and rejection of transplants, as well as improvement of bone fracture healing and improved bone grafts (abstract, columns 3 and 4, particularly column 4, lines 20, 30- 39). Deluca et al. teach the treatment may be transdermal, oral or parenteral in an amount from about 0.1μg/gm to about 50μg/gm of the composition

and may be administered in dosages of from about 0.1μg/day to about 50μg/day (column 4, lines 15-30). Deluca et al. teach 2MD can be formulated conveniently by any of the method well known in the art of pharmacy (column 18, lines 50-60).

Deluca et al. (US) do not teach increasing the rate of skeletal repair by stimulating osteoblast cells set forth in claim 1 and an immobilized, slow release formulation.

Deluca et al. (WO) teach that 2MD stimulates the osteoblasts at least 80 times more potent than $1,25\ (OH)_2D_2$ (pages 9-10, under INTERPRETATION OF DATA). Deluca et al. (WO) teach that 2MD can be use in hip and knee replacement surgery (abstract).

Bockman et al. teach that bone is formed by matrix-producing cells known as osteoblasts. Bockman et al. teach that osteoblast is responsible regulating the rate of formation and the architecture of newly formed bone (column 3, lines 31-57). Bockman et al. teach that compounds enhancing bone formation are suitable for use in the field of bone implants including both bone grafts and prosthetic devices. Bockman et al. teach that implants are routinely used to replace damaged or diseased joints and to support or replace weakened or lost bone. Bockman et al. teach that the implant can be used with a polymer that allows slow diffusion of the compounds that enhances bone growth for a suitable period of time (column 7, lines 50-60, column 8, lines 5-10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ 2MD for increasing the rate of skeletal repair by stimulating osteoblast cells to form new bone administering an effective amount of a

2MD in an immobilized, slow release such as bone implants comprising polymer because 2MD is well-known by Deluca et al. (US) for the treatment of healing and improving bone fracture where bone formation is desired and because 2MD is well known by Deluca et al. (WO) for also stimulating the osteoblasts which is responsible for regulating the rate of formation of new bone as taught by Bockman et al. One would have been motivated to employ 2MD for treatment of a condition where bone formation is desired such as bone fracture in order to achieve desired effects of 2MD having stimulating osteoblast cells that increase the rate of formation of new bone. There is a reasonable expectation of successfully increasing rate of repair in a bone fracture administering 2MD because 2MD stimulates osteoblast which enhances bone formation by increasing rate of new bone formation well known by cited references. It is obvious that the limitation of "skeletal repair" would also fall in this realm of bone repair.

The pharmaceutical forms as immobilized form and slow release form to be used to administer 2MD are all deemed obvious. Deluca et al. (US) teach that 2MD can be conveniently prepared by any the methods well known in the art of pharmacy and because formulating bone implants comprising slow diffusion polymer to deliver bone enhancing compounds are well known in the art as taught by Bockman et al.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

Conclusion

Claims 1, 8-22 and 29-32 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617